In re Appln. of Roelvink et al.
Application No. 09/617,569

Remarks

Summary of the Invention

The invention concerns a complex comprising a virion having a surface and a lumen and comprising viral capsid proteins, at least one non-native ligand displayed on the surface, which at least one ligand recognizes an epitope present on an immune effector cell, and at least one first nucleic acid encoding at least one first non-native antigen. (claims 1-18), a method of inoculating a mammal (claims 19-25), a method of immunizing a mammal (claims 26-32), and a pharmaceutical composition comprising a complex and a physiologically-acceptable carrier (claims 40-43).

Discussion of Office Action

Claim 20 is objected to because of language informalities. Claim 10 is rejected under 35 U.S.C § 112, second paragraph, as allegedly vague. Claims 1-32 and 40-43 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. The claims also are rejected under 35 U.S.C. § 102(b) and 103(a) on the basis of cited references.

Discussion of Amendments

Claims 24, 25, 31, and 32 are amended to change their dependencies. Claim 20 is amended to cure a typographical error – "mounds" is changed to "mounts." The language is supported in the specification (see, e.g., page 12, lines 20-24), and it adds no new matter to the application. No formal rejection, even under 35 U.S.C. § 112, first paragraph, has been made by virtue of this typographical error, and the Office Action clearly recognized the intent of the claim. Thus, the amendment is intended merely to clarify the claim to recite what applicants clearly intend to recite; it is not made for reasons of patentability. A copy of these claims, with markings indicating the amended language, is attached.

Discussion of Indefiniteness Rejection

Claim 10 is rejected under 35 U.S.C § 112, second paragraph, as allegedly vague. In particular, the Office Action questions the relationship of the liposome recited in the claim to the other elements of the complex. The specification notes that the complex can comprise adjuncts, such as one or more liposomes (see, e.g., page 9, lines 7-10). The adjunctive use of liposomes for delivery of substances to cells is known, and those of skill in the art will understand that the claim contemplates any adjunctive use of liposomes in the complex. Thus, the claim is considered to be definite to those of skill in the art.

Discussion of Enablement Rejection

Claims 1-32 and 40-43 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. The Office Action cites to several references as supporting its assertion that certain technical features of the claims are allegedly contradicted by the state of the art. A review of the references of record, however, reveals that the specification, in light of the state of the art, adequately enables the claims.

One assertion of non-enablement is the Office Action's allegation that administering a CD-40 ligand depresses the immune system (Office Action, page 4, citing Stein et al.). However, the CD-40 ligand actually can prime the immune effector cells, and thus enhance an immune response (see, e.g., Toes *et al.*, *Sem. Immunol.*, *10*, 443-48 (1998) (copy enclosed)). Another assertion of non-enablement is the Office Action's allegation that the state of the art recognized no effect of osteopontin on immune response (Office Action, page 4, citing Yu et al.). Yet, Ashkar et al. (reference AC of record) clearly identifies osteopontin (also called Eta-1) as "a key cytokine that sets the stage for efficient type-1 immune responses" (Abstract). Thus, contrary to the Office Action's assertion (page 5), the state of the art does not teach that the immune system is negatively effected by CD40L or osteopontin.

The Office Action further suggests that because different cytokines have different activities, the scope of the invention should be limited to only those cytokines that activate the immune system (Office Action, page 5). The only reference to "cytokines" in the claims appears in claims 18, 25, and 32. These claims specify that a "polypeptide" recited in superior claims (claims 16, 23, and 30, respectively) "is a cytokine." Because the "polypeptide" recited in these superior claims "activates an immune effector cell," so too does the cytokine recited in claims 18, 25, and 32. Thus, the claims already are drawn to activation of immune effector cells, and the concern expressed in the Office Action appears not to be n issue. In any event, as noted by the Janeway reference cited in the Office Action, it is known which cytokines activate immune effector cells, and which do not, and a vast body of literature on this subject no doubt exists. Thus the specification and the art as a whole clearly enable the claims, and the rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn.

Discussion of Anticipation Rejection

Claims 1, 2, 4-7, 9, 11-16, 19, 26, 27, 40, 42, and 43 are rejected as allegedly anticipated by Wickham et al. (U.S. Patent 5,846,782). The Office Action asserts that Wickham et al. discloses an adenovirus having a non-native RGD ligand and incorporating a passenger gene, such as HSV thymidine kinase.

While Wickham et al. once mentions the word "vaccination" (column 19, line 27), this mention appears in a context of a general discussion demonstrating that the state of the art recognized many ways of administering viruses. Taken in context, this passing reference certainly cannot be interpreted to disclose a method of eliciting an immune response, as the Office Action urges.

While Wickham et al. discloses an adenovirus having a ligand recognizing an epitope present on an immune-effector cell (an RGD domain), it does not disclose any other elements of the pending claims. For example, it does not identify any of the "passenger genes" (e.g., listed on column 14, lines 37-59) as antigens. Indeed, the patent describes such products as therapeutic genes, toxins, or prodrugs. The Office Action's assertion that the products of such passenger genes (e.g., HSV thymidine kinase) "can elicit a strong immune response" is not supported by the patent. Thus, Wickham et al. does not disclose all elements of the claims, and it does not explicitly anticipate them.

By relying on teachings extrinsic to the reference – i.e., that the passenger genes disclosed by Wickham et al. "can elicit a strong immune response" – rather than on the reference's express disclosures, the Office seeks to establish anticipation by inherency. "Inherency, however, cannot be established by possibilities, or even probabilities. The mere fact that a certain thing ***may*** result from a set of circumstances is not sufficient.." *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991). Rather, to support anticipation by inherency, inferred matter ***must necessarily be present*** in the references. In this respect, the very words of the Office Action – "***can elicit***" – demonstrate that Wickham et al. does not inherently anticipate the claims.

Because it neither expressly nor inherently discloses all elements of the claims, Wickham et al. does not anticipate them.

Discussion of Obviousness Rejection

Claims 8 and 10 are rejected as allegedly obvious over the combination of Wickham et al. and Hitt et al., and claims 18, 20-23, 25, 28-30, 32, and 41 are alleged to be obvious in view of these two references combined with Janeway.

As stated above in connection with the discussion of anticipation, the Wickham et al. patent does not provide a teaching sufficient to place the elements of claims 1 (upon which claims 8, 10, 18, 20-23, and 25 depend), 26 (upon which claims 28-30 and 32), or 40 (upon which claim 41 depends) in the art. Thus, its contribution to the proffered combination for obviousness purposes is insufficient to disclose needed elements of the claims. For this reason alone, the obviousness rejection should be withdrawn.

Hitt et al. disclose methods for human adenovirus vector construction. The reference makes no reference to any vector having two antigens (e.g., one encoded in the adenoviral

genome, the other on the surface of the virus), wherein the first and second antigens are the same. Nor does Hitt et al. disclose the complexing of an adenovirus with a liposome. Thus, Hitt supplies no teachings relevant to claims 8 and 10. In any event, the Office Action does not even allege that one of skill in the art would be motivated to combine Wickham et al. with Hitt et al. in any way, nor is there any such motivation. Thus, Hitt et al. and Wickham et al. do not combine to render claims 8 and 10 obvious.

Janeway discloses the activities of several cytokines, and the Office Action notes that the reference teaches that IFNγ augments MHC I and II responses. However, neither Janeway, nor Hitt et al., nor Wickham et al. provides any teaching to complex any cytokines with anything else. Indeed, the art supplies no motivation to one of ordinary skill to combine the teachings of these references in the precise manner required to arrive at the invention recited in claims 18, 20-23, 25, 28-30, 32, and 41.

The proffered combinations of references do not render any of claims 8, 10, 18, 20-23, 25, 28-30, 32, or 41 obvious, and the rejection should be withdrawn.

Conclusion

The application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the examination of the instant application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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